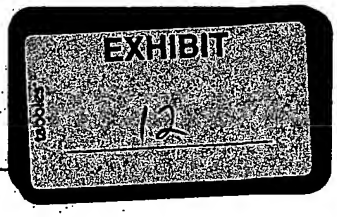
ELSEVIER SCIENCE
www.elsevier.com/locate/cardiosur

Cardiovascular Surgery, Vol. 9, No. 4, pp. 319–328, 2001

0967-2109/01 $20.00

PII: S0967-2109(00)00125-3



Expression of apoptosis-related proteins and structural features of cell death in explanted aortocoronary saphenous vein bypass grafts

A.Y. Wang*, Y.V. Bobryshev*, S.M. Cherian*, H. Liang*, D. Tran*, S.J. Inder*, R.S.A. Lord*, K.W.S. Ashwell† and A.E. Farnsworth‡

**Surgical Professorial Unit, St Vincent's Hospital, Victoria Street, Darlinghurst, Sydney, NSW 2010, Australia and †School of Anatomy, The University of New South Wales, Sydney, NSW 2052, Australia and ‡Department of Cardiothoracic Surgery, St Vincent's Hospital, Sydney, NSW 2010, Australia*

This study aimed to investigate the features of cell death occurring in aortocoronary saphenous vein bypass grafts. Human aortocoronary saphenous vein bypass grafts with angiographic luminal stenosis of >75% were explanted from 14 patients at redo coronary artery bypass grafting. Proteins associated with apoptotic pathways were identified immunohistochemically using antibodies to Bcl-2, Fas, BAX, p53 and CPP32. Cells undergoing DNA fragmentation were identified by terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling (TUNEL). DNA synthesis was investigated using the antibody to proliferating cell nuclear antigen (PCNA). Ultrastructural features of cell death were examined by electron microscopy. Anti-apoptotic (Bcl-2) and pro-apoptotic (Bax, p53, CPP32 and Fas) proteins were expressed throughout the graft wall, but marked differences in the characteristics of cell death were noted between atherosclerotic and non-atherosclerotic areas of the intima. In atherosclerotic areas, pro-apoptotic proteins were widely expressed, but ultrastructural analysis failed to identify cells showing typical features of apoptosis. In these areas, necrotic cells were frequently observed, with negative correlation of Bcl-2 expression with TUNEL. Pro-apoptotic proteins showed no correlation with TUNEL. In contrast, in non-atherosclerotic areas of vein grafts, the expression of both anti-apoptotic (Bcl-2) and pro-apoptotic proteins (p53, Bax and CPP32) correlated with TUNEL. In atherosclerotic areas, non-atherosclerotic intimal areas, and in the underlying media, the numbers of TUNEL+ cells correlated with PCNA positivity. Ultrastructurally, apoptotic bodies and features of necrosis were observed in non-atherosclerotic areas of grafts. The present observations indicate that in atherosclerotic areas, cell death occurs mainly by necrosis, while in non-atherosclerotic areas, cell death occurs by both necrosis and apoptosis. An imbalance between DNA fragmentation and DNA synthesis may contribute to graft instability and failure.

Keywords: apoptosis, atherosclerosis, cell death, coronary artery disease, necrosis, saphenous vein bypass grafts

Correspondence to: Dr Yuri V. Bobryshev. Tel: +61-2-9361-2354; fax: +61-2-9360-4424; e-mail: spu@stvincents.com.au